

APPLICANT(S): STEINER, Mitchell S. et al.  
SERIAL NO.: 10/747,686  
FILED: December 30, 2003  
Page 7

## **REMARKS**

### **Status of Claims**

Claims 1-3, 7-12 and 16-32 are pending in the application. Claims 1-3, 7-12 and 16-32 have been rejected. Claims 11, 16, 19, 21, 23-26, 28, and 30-32 have been amended. Support for the amended claims can be found in the Specification as originally filed, for example, on page 18, paragraphs 56-57, and in the examples. No new matter has been introduced.

Claims 1-10 and 12-15 have been canceled without prejudice or disclaimer. In making this cancellation without prejudice, Applicants reserve all rights in these claims to file divisional and/or continuation patent applications.

### **Double Patenting Rejections**

Claims 1-3, 7-12 and 16-32 were rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-3, 7, 45 and 54-67 of copending Application No. 10/611,056.

Applicants hereby offer to provide a terminal disclaimer upon indication by the Examiner of allowable claims.

Claims 1-3, 7-12 and 16-32 were rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-22 of copending Application No. 10/747,685.

Applicants hereby offer to provide a terminal disclaimer in view Application No. 10/747,685 of upon indication by the Examiner of allowable claims.

In the Office Action, the Examiner rejected claims 1-3, 7-12 and 16-32 under the judicially created doctrine of nonstatutory obviousness-type double patenting as allegedly being unpatentable over claims 1-17, 1-34, 1-20, 1-17, 1-19, 1-34 and 1-63 of US Patent Nos. 6,413,534, 6,413,533, 5,413,535, 6,410,043, 6,265,448, 6,632,447 and 6,899,888, respectively.

APPLICANT(S): STEINER, Mitchell S. et al.  
SERIAL NO.: 10/747,686  
FILED: December 30, 2003  
Page 8

Applicants respectfully wish to draw the Examiner's attention to a typographical error. US Patent No. 5,413,535 is in fact 6,413,535.

Applicants hereby offer to provide a terminal disclaimer with respect to US Patent Nos. 6,413,534, 6,413,533, 6,413,535, 6,410,043, 6,265,448, 6,632,447 and 6,899,888 upon indication by the Examiner of allowable claims.

### CLAIM REJECTIONS

#### 35 U.S.C. § 112 Rejections

Applicants thank the Examiner for acknowledging that claims to the use of 60 mg of Toremifene in treating PIN are enabled.

The Examiner rejected claims 1-3, 7-12 and 16-32 under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement.

The Examiner alleged that the specification does not enable all compounds represented by formula I. Applicants disagree. The compounds are known in the art (see, for example, US Patent No. 6,265,448). The core compound is used clinically, and the genus represents the core compound and its biologically active variants and metabolites. However, in order to advance prosecution, Applicants have amended claims to claim "a method of reducing the incidence of pre-malignant lesions of prostate cancer in a human comprising the step of administering to the human a pharmaceutical composition comprising 60 mg of Toremifene or a metabolite thereof, wherein the metabolite is 4-chloro-1,2-diphenyl-1-[4-[2-(N-methylamino) ethoxy] phenyl]-1-butene; 4-chloro-1,2-diphenyl-1-[4-[2-(N,N-diethylamino) ethoxy]phenyl]-1-butene; 4-chloro-1,2-diphenyl-1-[4 (aminoethoxy)]-1-butene; 4-chloro-1-(4-hydroxyphenyl)-1-[4-[2-(N,N-dimethylamino) ethoxy] phenyl]-2-phenyl-1-butene; 4-chloro-1-(4-hydroxyphenyl)-1-[4-[2-(N-methylamino)ethoxy] phenyl]-2-phenyl-1-butene; or 4-chloro-1,2-bis(4-hydroxyphenyl)-1-[4-[2-(N,N-dimethylamino)ethoxy]phenyl]-1-butene".

The Examiner further alleged that claims to inhibiting PIN/HGPIN at any stage and in all cases lack enablement. Applicants disagree. However, in order to expedite prosecution, claims 1-10 have been canceled, rendering the rejection moot. Applicants reserve all rights to file a divisional or continuation application with claims indicated as cancelled.

APPLICANT(S): STEINER, Mitchell S. et al.  
SERIAL NO.: 10/747,686  
FILED: December 30, 2003  
Page 9

The Examiner alleged that the subject application fails to show a correlation between all the conditions associated with PIN claimed as being treated/prevented/suppressed by the compounds of the instant claims. Applicants disagree. The subject application describes a method of treating PIN, and is not directed to conditions associated with PIN.

The Examiner alleged that it is necessary to determine the predisposing factors to PIN prior to using the methods of the subject application. Applicants disagree. Instant claims are to reducing the incidence of PIN and not to latency. PIN represents a discrete disease state, separate from frank neoplasia. PIN is not prostate cancer (Foster C.S *et al.*, 2000). Moreover, PIN does not always result in prostate cancer, and not all prostate cancer arises from PIN. Other lesions, such as ASAP (C.K. Moore. J. Urol 173:70-72 (2005)), post-atrophic hyperplasia (PAH) (A.N. Vis BJU International 88:147-157 (2001)), atypical adenomatous hyperplasia (AAH) and proliferative inflammatory atrophy (PIA) (W.G. Nelson J Urol 172:S6-S12 (2004)), may result in prostate cancer. Even in prostates that have cancer, the chance of having PIN is 82% and 18% have no evidence of PIN (D. Bostwick Seminars in Urologic Oncology, 17:187-198 (1999)).

The Examiner further alleged that there can be no treatment for all conditions associated with PIN/HGPIN and other related conditions. Applicants disagree. Applicants maintain that the instant claims are directed only to a method of reducing the incidence of, or treating, PIN, or preventing lesions of prostate cancer. Accordingly, Applicants request withdrawal of the rejection.

The Examiner rejected claims 1-3, 7-12 and 16-32 under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement.

The Examiner alleged that the specification as filed fails to clearly describe metabolites of the compound of formula (I) suppressing or inhibiting the incidence of premalignant lesions of prostate cancer. The instant claims are directed to a method of treating or reducing the incidence of PIN in a subject with 60 mg of Toremifene or a metabolite thereof. The term metabolite is an art-recognized term and refers, *inter alia*, to any intermediate or product resulting from metabolism. Metabolites of Toremifene are named on page 18, paragraph 57 of the Specification as originally filed. Accordingly, Applicants request withdrawal of the rejection.

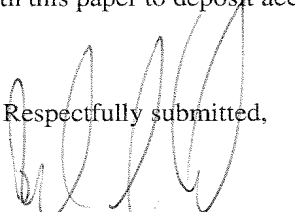
APPLICANT(S): STEINER, Mitchell S. et al.  
SERIAL NO.: 10/747,686  
FILED: December 30, 2003  
Page 10

In view of the foregoing amendments and remarks, the pending claims are deemed to be allowable. Their favorable reconsideration and allowance is respectfully requested.

Should the Examiner have any question or comment as to the form, content or entry of this Amendment, the Examiner is requested to contact the undersigned at the telephone number below. Similarly, if there are any further issues yet to be resolved to advance the prosecution of this application to issue, the Examiner is requested to telephone the undersigned counsel.

Please charge any fees associated with this paper to deposit account No. 50-3355.

Respectfully submitted,



Mark S. Cohen  
Attorney/Agent for Applicant(s)  
Registration No. 42,425

Dated: September 25, 2008

**Pearl Cohen Zedek Latzer, LLP**  
1500 Broadway, 12th Floor  
New York, New York 10036  
Tel: (646) 878-0800  
Fax: (646) 878-0801